

## REMARKS

With the entry of the present amendments, Claims 1-5, 7 and 8 are pending in the application. Claims 1, 7 and 8 have been amended. Claims 6, 9, and 10 have been canceled. Support for the amendments to Claim 1 may be found throughout the application as filed, including on page 5, lines 8-13. Claims 7 and 8 have been amended to change their dependency from Claim 6 (now cancelled) to Claim 1.

In view of the following remarks, reconsideration and withdrawal of the rejections to the application in the Office Action is respectfully requested.

### I. *Rejection of Claims under 35 U.S.C. § 103(a).*

Pending claims 1-5, 7 and 8 stand rejected under 35 U.S.C. § 103(a) as anticipated by Fiedorowicz et al. (hereinafter “Fiedorowicz”) in view of Reed et al. (hereinafter “Reed”) or Indig, “Photochemistry of triarylmethane dyes bound to proteins” (hereinafter “Indig”). Applicant respectfully traverses.

In order to establish a prima facie case of obviousness, three criteria must be met:

- (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to combine reference teachings;
- (2) the suggestion or motivation must be based on a reasonable expectation of success; and
- (3) the references must teach or suggest all of the claim limitations. (MPEP 2142) The Examiner has failed to met at least criteria (1) and (2).

“In determining the Patent Office case for obviousness, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification.” (MPEP 2143.01) The teachings of both Indig and Reed are insufficient to motivate one of ordinary skill in the art to use crystal violet in the photodynamic therapy methods of Fiedorowicz.

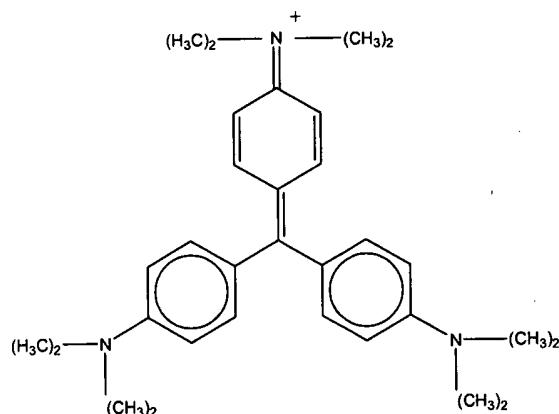
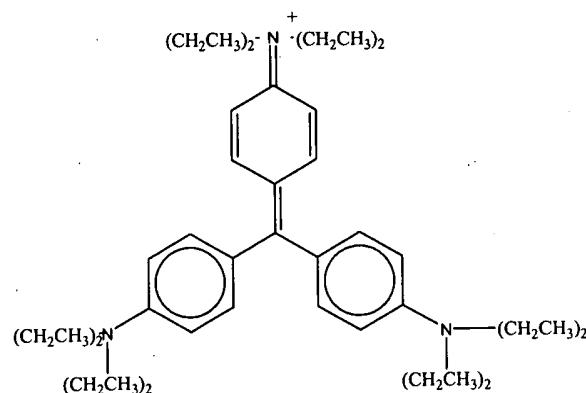
As one of ordinary skill in the art would recognize, a photosensitizer for use in photodynamic therapy, must exhibit selective killing of neoplastic tissues (i.e., cancer cells). Claim 1 has been amended to recite this important feature. This fact is explicitly acknowledged in Fiedorowicz and Indig. Specifically, Fiedorowicz states, "Photodynamic therapy (PDT) of cancer is based on the administration of photosensitizing drugs that are taken by and/or retained in tumor cells to a higher extent than in normal cells." (See, Introduction on page 855.) Similarly, Indig teaches, "In the design of new sensitizers for use in PDT, the ideal candidates should display the following properties: ...good cell-penetrating properties and selective retention by neoplastic tissues . . ." (See Concluding Remarks on pare 234.) It follows that one or ordinary skill in the art would only be motivated to use compounds that are known to selectively target tumor cells in photodynamic therapy. Neither Indig nor Reed teaches that crystal violet has the selectivity that is required for a photodynamic therapy agent.

The Examiner alleges that Indig teaches, "photoreactive compounds such as Crystal Violet ... are efficacious in the treatment of neoplastic diseases." However, Applicant respectfully submits that Indig does not actually teach that crystal violet is efficacious in the treatment of neoplastic diseases. Rather, Indig merely teaches that crystal violet might have some of the characteristics that are necessary, *but not sufficient*, for a photodynamic therapy agent. Specifically, Indig teaches that crystal violet molecules complexed with bovine serum albumin strongly absorb at relatively long wavelengths, become transparent to excitation light after photoreaction, and remain photoreactive in the absence of oxygen. (See Concluding Remarks on pages 234-235.) Indig is silent regarding the ability of crystal violet to *selectively* target and kill cancer cells. In fact, the studies described in Indig are not designed to provide any information regarding crystal violet's ability to *selectively* target and kill cancer cells. Indeed, there are no cells, cancerous or otherwise, involved in the studies of Indig at all. Therefore, because Indig fails to demonstrate that crystal violet has the selectivity that is critical for a photodynamic therapy agent, one of ordinary skill in the art would not be motivated by the teachings of Indig to use crystal violet in the photodynamic therapy methods of Fiedorowicz. For

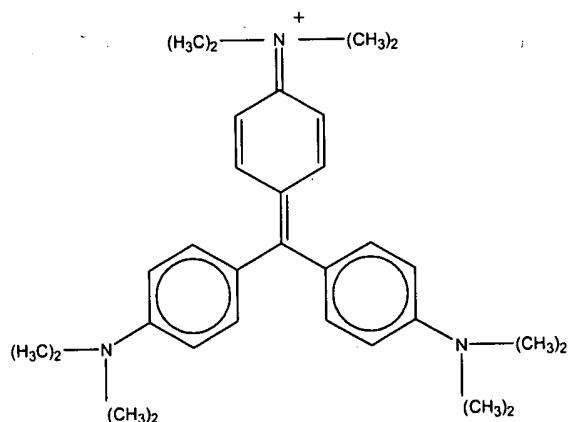
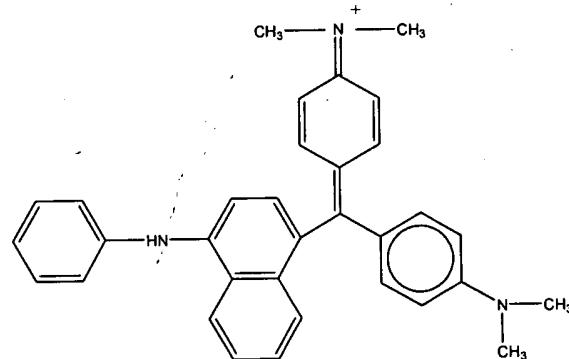
this reason, Applicant respectfully requests that the rejection based on Fiedorowicz and Indig be withdrawn.

Reed provides even less motivation than Indig to use crystal violet in photodynamic therapy. Reed describes the use of crystal violet as a conventional chemotherapeutic agent. Conventional chemotherapeutic agents are substantially different from the *photochemotherapeutic* agents disclosed in Fiedorowicz because they rely upon the systemic toxicity of the compounds, rather than the creation of photoproducts, to cause cell death. Therefore, the efficacy of crystal violet as a conventional chemotherapy agent does not provide any motivation to use crystal violet as a *photochemotherapy* agent, as described by Fiedorowicz. Moreover, Fiedorowicz does not teach that crystal violet possesses the required selectivity for use in photodynamic therapy. Indeed, the fact that the crystal violet of Reed resulted in a substantial number of premature deaths would suggest that selective targeting of cancerous cells was not achieved. Therefore, Reed provides no suggestion or motivation to use crystal violet in the photodynamic therapy methods of Fiedorowicz and Applicant respectfully requests that this rejection be withdrawn.

Applicant further submits that even if the combined teachings of Fiedorowicz and Indig or Reed were to motivate one to use crystal violet in photodynamic therapy, that motivation would not be based on a reasonable expectation of success. Evidence that the art in question is unpredictable may be used to show that there was no reasonable expectation of success. (MPEP 2143.02) The disclosure of the pending application establishes that the ability of a cationic dye to selectively kill cancer cells is highly unpredictable and varies dramatically with even small changes in the structure of the dye. For example, the studies described in the present application demonstrate that although crystal violet demonstrates good selectivity toward cancer cells, ethyl violet shows poor selectivity. (See, for example, Figure 3 and associated discussion on page 15.) This is particularly striking in view of the fact that crystal violet and ethyl violet have very similar structures, differing only by the replacement of the methyl groups on crystal violet with ethyl groups, as shown in the structures below:

Crystal VioletEthyl Violet

It follows that if two cationic dyes as similar in structure as crystal violet and ethyl violet can exhibit such different selectivity characteristics, it would be unreasonable to expect that one of ordinary skill in the art could reasonably expect to predict the selectivity behavior of crystal violet based on Fiedorowicz's discussion of Victoria Blue BO, which has a structure quite dissimilar to crystal violet, as shown below:

Crystal VioletVictoria Blue BO

For this additional reason, Applicant respectfully submits that the Examiner has failed to establish a prima facie case of obviousness and respectfully request that the rejection be withdrawn.

***II. Double Patenting Rejection.***

Pending Claim 1-5, 7 and 8 stand rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over Claims 1-26 of U.S. Patent No. 6,914,078. As noted in the Office Action, a Terminal Disclaimer may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground.

Enclosed is a copy of a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c) and 37 C.F.R. § 3.73(b). This Terminal Disclaimer was originally filed with Applicant's response to the previous Office Action, which was mailed to the U.S. Patent Office on November 29, 2005. It is respectfully submitted that this Terminal Disclaimer overcomes the rejections of Claims 1-5, 7 and 8. Therefore, Applicant respectfully requests that the Examiner withdraw the rejection of Claims 1-5, 7 and 8 based on nonstatutory obviousness-type double patenting and allow this application to issue. The filing of the enclosed Terminal Disclaimer should not be construed as an admission by the Applicant that the rejection of claims 1-5, 7 and 8 under the judicially created doctrine of obviousness-type double patenting is appropriate.

Applicant believes the Examiner may have simply overlooked the previously filed Terminal Disclaimer in making the present double patenting rejection. However, if the Terminal Disclaimer is in any way deficient, Applicant requests that the Examiner clarify the deficiency.

In view of the foregoing remarks Applicant respectfully submits that all the claims remaining in the application are condition for allowance and favorable action thereon is respectfully solicited. The Examiner is invited contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date August 18, 2006

FOLEY & LARDNER LLP  
Customer Number: 23524  
Telephone: (608) 258-4305  
Facsimile: (608) 258-4258

By



Michelle Manning  
Attorney for Applicant  
Registration No. 50,592